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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,131	11/30/2001	Daniel R. Soppet	PZ037P1C1	3384

22195 7590 12/01/2004

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,131	SOPPET ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11-13,17-20,23 and 25-74* is/are pending in the application.

4a) Of the above claim(s) *1,13,17-20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12 and 25-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 9/2/04, have been entered in full.

Claims 1, 13, 17-20, 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/2/04.

The traversal is on the grounds that a search of Groups I-VIII would not be a serious burden on the examiner. This is not found persuasive for the following reasons:
Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) or distinct as claimed (see MPEP § 806.05- §806.05(I)): and
(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search. These criteria were met in the above restriction. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. In the instant case, for example, although a search of the polypeptides of Group II would overlap a search of the polynucleotides of Group I, the two searches would not be coextensive. In many instances, a protein will have been known in the art before the DNA has been discovered that encodes the protein. Often the protein will be known by a name different than the name given the protein after the cloning of the nucleic acid - and may even be associated with a completely different activity than that ascribed to it when the

nucleic acid was cloned. Thus, Groups VIII require divergent searches, and to search all inventions would be burdensome. Therefore, the restriction is maintained and made final. Additionally, Applicant is reminded that the claims are being examined only to the extent that they read on the elected SEQ ID NO: 65.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c)., see page 19 of the Declaration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons:

The claims require a polynucleotide of SEQ ID NO: X encoding a polypeptide of SEQ ID NO: Y, or variants. The specification at page 91 defines SEQ ID NO: X and Y as follows: "SEQ ID NO:X (where X may be any of the polynucleotide sequences disclosed in the sequence listing) and the translated SEQ ID NO:Y (where Y may be any of the polypeptide sequences disclosed in the sequence listing)". This definition is by way of example and does not indicate which sequences are excluded from the claims, if any. The

same is true for a polynucleotide encoded by a ATCC Deposit Z and for variants at page 96. Thus the artisan cannot be reasonably appraised of the bounds of the claims.

Claim 11(b) requires "having biological activity". This phrase renders the claims indefinite for two reasons. First it is unclear if the phrase is mint to relate to the "polypeptide fragment" or to the "encoded sequence" or to both. Second, there is no definition of the phrase in the specification, and nor is such recognized in the art that clearly sets forth the bounds of the claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11, 12 and 25-74 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The claims are directed to polypeptides of SEQ ID NO: 65. The specification puts forth that the polynucleotides and polypeptides could be used as tissue specific or chromosomal markers, pages 31 and 165. Consistent with current examination guidelines, use as a tissue specific and/or chromosomal marker is not considered to be a substantial utility. Most every polypeptide exhibits some tissue specific pattern of expression and most every gene encoding a polypeptide is localized to some region of a chromosome. However, without some assertion that the tissue or chromosomal localization can be used to practice a particular substantial utility, as in a marker for a particular disease state, the use of the polypeptides or polynucleotides as tissue or chromosomal marker does not constitute a substantial utility. It is not a specific use because any integral membrane protein could be used in exactly the same way. Further, many polypeptides

are known in the art, yet the polypeptides have no known function or known ligands. Any of these orphan clones could be used in the manner described in the specification for the claimed polypeptide.

A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of treating an unspecified disease or condition with a material that has no particular correlation with a disease would not constitute a substantial utility. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

The specification puts forth that the polypeptide could be involved in any number of disparate disease states, and could therefore be used as a diagnostic or therapeutic agent (see pages 32, 166 and 173, for example). A stated belief that a correlation exists between the polypeptides and any number of diseases is not sufficient guidance to use the claimed polynucleotides to treat and/or diagnosis a particular disease; it merely defines a starting point for further research and investigation.

The specification puts forth that the polypeptide and/or polynucleotides could be used in forensic biology (page 172). However the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual. While one of skill in the art would appreciate that there may exist polymorphisms in the disclosed sequences, this amounts to

nothing more than an invitation to the skilled artisan to try and find such polymorphisms if they exist.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids.

Claims 11, 12 and 25-74 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Furthermore, the claims encompass polypeptide variants of the polypeptide of SEQ ID NO: 65, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 65; should Applicant establish a specific and substantial utility for the claimed polynucleotides, Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 65, but which still retain a desired property of the polypeptide of SEQ ID NO: 65. The claims require polypeptides comprising only portions of SEQ ID NO: 65 and polypeptides having a recited degree of identity with SEQ ID NO: 65. Thus, the vast majority of polypeptides are amino acid sequence variants of SEQ ID NO: 65, i.e. amino acid substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 65, yet the specification has failed to teach one of skill in the art

which amino acid substitutions, deletions or insertions to make. Furthermore, Applicant has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 65 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 65 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 65 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 65, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 65. Conversely, if a protein variant of SEQ ID NO: 65 need not have a disclosed property, the specification has failed to teach how to use such a variant.

The specification has failed to provide an activity of SEQ ID NO: 65 to be used to evaluate the claimed variants for usefulness. The specification has not provided a working example of the use of a variant of the polypeptide of SEQ ID NO: 65 nor sufficient guidance so as to enable one of skill in the art to make such a variant. The specification has failed to teach which amino acids of SEQ ID NO: 65 could be modified so as to produce a polypeptide that is not identical to SEQ ID NO: 65 and yet still retain the activity of the polypeptide of SEQ ID NO: 65 - which has apparently not been disclosed.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any

given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 65 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely

an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to generate the infinite number of variant recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 11, 12 and 25-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polypeptide of SEQ ID NO: 65, yet the claims encompass polypeptides not described in the specification, i.e. proteins which comprise only portions of SEQ ID NO: 65, e.g. sequences from other species, mutated sequences, allelic variants, or

sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the amino acid positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of a single polypeptide, that of SEQ ID NO: 65 with no instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence SEQ ID NO: 65, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

The instant claims are not directed to that which is disclosed as essential to the invention, i.e. something that is homologous to the parent SEQ ID NO: 65 and has the function the parent protein. Thus, with the exception of the of the polypeptide of SEQ ID NO: 65, the skilled artisan cannot envision encompassed variants. Therefore, only a polypeptide of SEQ ID NO: 65, and polypeptides *consisting* of fragments thereof, or polypeptides consisting of fragments thereof and

heterologous sequences (e.g. carrier or tag sequences), but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. As discussed above the claims read on essentially any protein that could be considered a SEQ ID NO: Y or a variant of SEQ ID NO: 65. Alexander teach such a protein, MHr and MHr with sequential deletions MHr (79-84), see the Abstract.

Claims 11 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No: 6020161 filed Oct 22, 1997.

6020161 discloses a polypeptide that has an overall 30% sequence identity with the instant SEQ ID NO: 65, see sequence alignment below, and would therefore be considered a variant of SEQ ID NO: 65. Fragments are also disclosed, i.e. sequential deletions, see col 15.

```
US-08-955-937A-2
; Sequence 2, Application US/08955937A
; Patent No. 6020161
;  GENERAL INFORMATION:
;    APPLICANT:  WU, SHUJIAN
;    APPLICANT:  SWEET, RAYMOND
;    APPLICANT:  TRUNEH, ALEMSEGED
;    TITLE OF INVENTION:  PIGR-1, A MEMBER OF IMMUNOGLOBULIN
;    TITLE OF INVENTION:  GENE SUPERFAMILY
;    NUMBER OF SEQUENCES:  14
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  RATNER & PRESTIA
;      STREET:  P.O. BOX 980
;      CITY:  VALLEY FORGE
;      STATE:  PA
;      COUNTRY:  USA
;      ZIP:  19482
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Diskette
;      COMPUTER:  IBM Compatible
;      OPERATING SYSTEM:  DOS
;      SOFTWARE:  FastSEQ for Windows Version 2.0
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/955,937A
;      FILING DATE:  17-OCT-1997
;      CLASSIFICATION:  435
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  60/056,152
;      FILING DATE:  19-AUG-1997
;    ATTORNEY/AGENT INFORMATION:
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;      REGISTRATION NUMBER:  23,031
;      REFERENCE/DOCKET NUMBER:  GH-70228
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  610-407-0700
;      TELEFAX:  610-407-0701
;      TELEX:  846169
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  201 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-955-937A-2

  Query Match           30.1%;  Score 451.5;  DB 3;  Length 201;
  Best Local Similarity  49.8%;  Pred. No. 1.1e-38;
  Matches  103;  Conservative   22;  Mismatches   57;  Indels   25;  Gaps    8;

Qy          8 LLLFWLSGYSIATQITGPTTVNGLERGSLTVQCVYRSGWETYLKWWCRGAIWRDCKILVK 67
              |||  |||      | || :|   |:||||||| |: |||||:||||||  |  ||||::
Db          7 LLLLSLSG---CFSIQGPESVRAPEQGSLTVQCHYKQGWETYIKWWCRGVRWDTCKILIE 63

Qy         68 TSGGSEQEVKRDRVSIKDNQKNRTFTVTMEDLMKTDADTYWCGIEKTGNDLGVTVQVTIDP 127
              | ||||  | ||||||||||:||||||| | : ||| |||||| | |||  |:| :||
Db         64 TRGSEQGEKSDRVSIKDNQKDRTFTVTMEGLRRDDADVYWCGIERRGPDLGTQVKVIVDP 123

Qy        128 APVTQEETSSSPT------LTGHHLDNRHKLLKLSVLLPLIFTIXLLLLVAASLLAWRMM 181
                    |:||||        | |  | | :| : | :|:     ||:|| | |  |  :
Db        124 EGAA-STTASSPTNSNMAVFIGSHKRN-HYMLLVFVKVPI-----LLILVTAIL--W--L 172

Qy        182 KYQQKAAGMSPEQVL-----QPLEGDL 203
              |  |:      || :     :||  |:
Db        173 KGSQRVPEEPGEQPIYMNFSEPLTKDM 199
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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

November 28, 2004